

EXHIBIT F

INDICATION AND SURGICAL TREATMENT OF MIDURETHRAL SLING COMPLICATIONS: A MULTICENTER STUDY

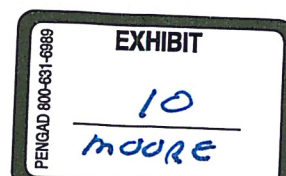
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Introduction: Although midurethral sling can be performed on an outpatient basis and is minimally invasive, it can be associated with postoperative complications such as new onset vaginal pain, dyspareunia, lower abdominal pain and even leg or thigh pain depending on the type of synthetic mesh sling procedure utilized: 1) retropubic (RP) sling 2) transobturator (TOT) or 3) single incision sling (SIS).

Objectives: 1) To evaluate the most common indication for sling removal in patients with synthetic mesh slings. 2) Discuss the location of pain and the incidence of the location for each of the three types of synthetic sling procedure. 3) Compare the indications for surgery for mesh removal between the three different types of synthetic mesh slings.

Methods: A retrospective chart review of all patients who underwent surgical removal of sling related complications from 2011 to 2013 at three tertiary referral centers in the Southeast United States. We included all women who underwent sling removal. The database was queried to identify potential subjects, the types of procedure performed, types of mid-urethral sling and their demographic data. Data was analyzed by using chi-square test for categorical data, and Student's t-test and Wilcoxon Rank Sum test for continuous data. The measure of effect was determined by logistic regression analysis.

Results: There were 337 sling complications followed the IUGA/ICS mesh complication classification. Retropubic sling (RP) was more likely to have urinary tract complications (category 4) and intra-abdominal site complications (S5) than other slings (Table 1). Main indications for RP revision/removal were pain (53.9%), dyspareunia (14.6%), and urinary retention (6.9%) respectively. Main indications for transobturator tape (TOT) sling removal were pain (66.0%), dyspareunia (10.7%), and urinary retention (5.3%). Main indications for single incision sling (SIS) removal were were pain (57.5%), dyspareunia (14.6%), and erosion/extrusion (6.4%). Urinary retention was more likely to be an indication for removal in RP group ($p=0.049$). Of those 286 sling/mesh removed, 106 (37.1%) accounted for RP, 131 (45.8%) TOT, and 44 (15.4%) SIS. Table 2 shows pain location among patients who underwent surgical treatment due to pain. Vaginal pain was the most common site across sling types. Twenty-one percent of TOT group had groin pain which was 5 times higher risk than RP group (OR 5.3, 95%CI 1.5- 18.7). RP group was 3 times more likely to have suprapubic pain than TOT group (OR 2.97, 95% CI 1.3- 7.0). Fifty percent of RP was removed laparoscopically. Fifteen percent of TOT had either unilateral or bilateral groin mesh removal. Among 11 slings were removed transurethrally, 8 of them were SIS. Six slings were removed from bladder and 5 of them were RP. The median estimated blood loss was 50 cc. (range 0-800). For RP sling removal, laparoscopic combined with vaginal approach had more blood loss compared to vaginal approach alone (mean 87.2 vs. 55.0 cc, $p<0.001$). For TOT removal, groin removal combined with vaginal approach had more blood loss compared with vaginal approach alone (mean 79.7 vs. 59.1 cc, $p=0.008$). Two patients who underwent laparoscopic RP sling removal received blood transfusion and one patient



had retroperitoneal hematoma required reoperation. Among TOT removal, three patients had intraoperative urethral injury and 2 patients had excessive blood loss.

Conclusion: The most common indication for sling removal was vaginal pain. RP sling has higher risk of suprapubic pain and TOT sling has higher risk of groin pain. Patients suffering from only vaginal pain underwent only vaginal removal of the sling. Patients suffering from groin pain were more often subjected to groin dissection to remove the TOT sling and patients suffering from suprapubic pain were subjected to laparoscopy to remove the arms of the RP sling. Patients with a history of SIS may have a higher incidence of urethral erosion compared to TOT or RP slings. TOT removal has higher intraoperative complications. Total sling removal for RP slings may increase the risk of blood transfusion.

Table 1- IUGA/ICS classification of complications related directly to the midurethral sling in female pelvic reconstructive surgery (286 sling removed, 337 complication classified)

	sling (n=337)			
	RP (n=133)	TOT (150)	SIS (n=47)	P-value
Category				
1. Vaginal: no epithelial separation	85 (65.38)	101 (67.79)	33 (70.21)	0.814
2. Vaginal: smaller ≤ 1 cm exposure	12 (9.23)	15 (10.07)	10 (21.28)	0.067
3. Vaginal: larger > 1 cm exposure, or any extrusion	8 (6.15)	14 (9.40)	1 (2.13)	0.207
4. Urinary tract: compromise or perforation including prosthesis (graft) perforation and fistula	13 (10.00)	4 (2.68)	2 (4.26)	0.030
5. Rectal or bowel: compromise or perforation including prosthesis (graft) perforation and fistula	2 (1.54)	0 (0)	0 (0)	0.219
6. Skin or musculoskeletal: complications including discharge pain lump or sinus tract formation	9 (6.92)	15 (10.07)	1 (2.13)	0.187
7. Patient: compromise including hematoma or systemic compromise	1 (0.77)	0 (0)	0 (0)	0.470
Time (Clinical diagnosed)				
T1: Intraoperative to 48 hours	1 (0.77)	0 (0)	0 (0)	0.470
T2: 48 hours to 2 months	4 (3.08)	4 (2.68)	0 (0)	0.490
T3: 2 months to 12 months	15 (11.54)	12 (8.05)	4 (8.51)	0.594
T4: over 12 months	110 (84.62)	133 (89.26)	43 (91.49)	0.348
Site				
S1: vaginal: area of suture line	19 (14.62)	18 (12.08)	10 (21.28)	0.293
S2: vaginal: away from suture line	59 (45.38)	86 (57.72)	28 (59.57)	0.075
S3: Trocar passage	7 (5.38)	11 (7.38)	2 (4.26)	0.664
S4: other skin or musculoskeletal site	19 (14.62)	33 (22.15)	7 (14.89)	0.219
S5: Intra-abdominal	26 (20.00)	1 (0.67)	0 (0)	<0.001

Table 2- Type of sling removed due to pain, n (%)

Pain location	sling (n=179)			
	RP (n=63)	TOT (91)	SIS (n=25)	P-value
vagina	29 (46.03)	48 (52.75)	14 (56.00)	0.580
paraurethra	3 (4.76)	5 (5.49)	3 (12.00)	0.403
thigh	0 (0)	2 (2.20)	0 (0)	0.376
groin	3 (4.76)	19 (20.88)	2 (8.00)	0.012
suprapubic/ lower abdomen	17 (26.98)	10 (10.99)	4 (16.00)	0.037
abdomen	11 (17.46)	7 (7.69)	2 (8.00)	0.150